PSJ2 Exh 45

FINAL MATERIAL

PROVIDING RELIEF

PREVENTING ABUSE

A reference guide to controlled substance prescribing practices

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AT PURDUE PHARMA, WE ARE COMMITTED TO:

- Ensuring that people with legitimate medical need have access to appropriate analgesic therapy
- Providing educational resources to both the medical and law enforcement communities to help ensure proper use and availability of these medications
- Helping to prevent the abuse and diversion of these medications

This quick reference guide features a brief history of opioid use, Drug Enforcement Administration (DEA) schedules of controlled substances, and meaningful definitions related to the use of opioids in the treatment of pain. It also provides information on how to identify patients with potential abuse or diversion problems, so you can help them seek appropriate treatment. This is intended to serve as a general guide, and should not be used as a sole resource or in lieu of clinical or professional judgment.

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PROMOTING PAIN RELIEF AND PREVENTING ABUSE OF PAIN MEDICATIONS: A CRITICAL BALANCING ACT[1]

October 23, 2001

A JOINT STATEMENT FROM 21 HEALTH ORGANIZATIONS* AND THE DRUG ENFORCEMENT ADMINISTRATION

As representatives of the health care community and law enforcement, we are working together to prevent abuse of prescription pain medications while ensuring that they remain available for patients in need.

Both healthcare professionals, and law enforcement and regulatory personnel, share a responsibility for ensuring that prescription pain medications are available to the patients who need them and for preventing these drugs from becoming a source of harm or abuse. We all must ensure that accurate information about both the legitimate use and the abuse of prescription pain medications is made available. The roles of both health professionals and law enforcement personnel in maintaining this essential balance between patient care and diversion prevention are critical.

Preventing drug abuse is an important societal goal, but there is consensus, by law enforcement agencies, health care practitioners, and patient advocates alike, that it should not hinder patients' ability to receive the care they need and deserve.

This consensus statement is necessary based on the following facts:

- Undertreatment of pain is a serious problem in the United States, including pain among patients with chronic conditions and those who are critically ill or near death. Effective pain management is an integral and important aspect of quality medical care, and pain should be treated aggressively.
- For many patients, opioid analgesics—when used as recommended by established pain management guidelines—are the most effective way to treat their pain, and often the only treatment option that provides significant relief.

- Because opioids are one of several types of controlled substances that have potential for abuse, they are carefully regulated by the Drug Enforcement Administration and other state agencies. For example, a physician must be licensed by State medical authorities and registered with the DEA before prescribing a controlled substance.
- In spite of regulatory controls, drug abusers obtain these and other prescription medications by diverting them from legitimate channels in several ways, including fraud, theft, forged prescriptions, and via unscrupulous health professionals.
- Drug abuse is a serious problem. Those who legally manufacture, distribute, prescribe and dispense controlled substances must be mindful of and have respect for their inherent abuse potential. Focusing only on the abuse potential of a drug, however, could erroneously lead to the conclusion that these medications should be avoided when medically indicated—generating a sense of fear rather than respect for their legitimate properties.
- Helping doctors, nurses, pharmacists, other healthcare professionals, law enforcement personnel and the general public become more aware of both the use and abuse of pain medications will enable all of us to make proper and wise decisions regarding the treatment of pain.

***American Academy of Family Physicians; American Academy of Hospice and Palliative Medicine; American Academy of Pain Medicine; American Alliance of Cancer Pain Initiatives; American Cancer Society; American Medical Association; American Pain Foundation; American Pain Society; American Pharmaceutical Association; American Society of Anesthesiologists; American Society of Law, Medicine & Ethics; American Society of Pain Management Nurses; American Society of Regional Anesthesia and Pain Medicine; Community-State Partnerships to Improve End-of-Life Care; Drug Enforcement Administration; Last Acts; Midwest Bioethics Center; National Academy of Elder Law Attorneys; National Hospice and Palliative Care Organization; Oncology Nursing Society; Partnership for Caring, Inc.; University of Wisconsin Pain & Policy Studies Group.**

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CONSIDERATIONS IN CONTROLLED SUBSTANCE ABUSE

FACTS ABOUT ADDICTION:

"Misunderstanding of addiction and mislabeling of patients as addicts result in unnecessary withholding of opioid medications."[2]

—The American Academy of Pain Medicine and American Pain Society

"A history of substance abuse does not absolutely preclude the use of opioids, but it does warrant extra caution. Active or recent substance abuse suggests that another strategy is preferable....Hesitate, too, when patients live with substance abusers or have an otherwise chaotic home life."[3]

—Ellison NM, et al. *Patient Care*

IMPEDIMENTS TO PAIN MANAGEMENT:

"The impediments [to pain management] include lack of legal recognition of the medical value of opioids, limitations on prescribing and dispensing, exclusion of substance abusers from prescriptions for pain medications, physician concern about discipline, and the confusion of physical dependence with addiction in both policy and practice."[5]

—American Bar Association Commission on Legal Problems of the Elderly (www.abanet.org)

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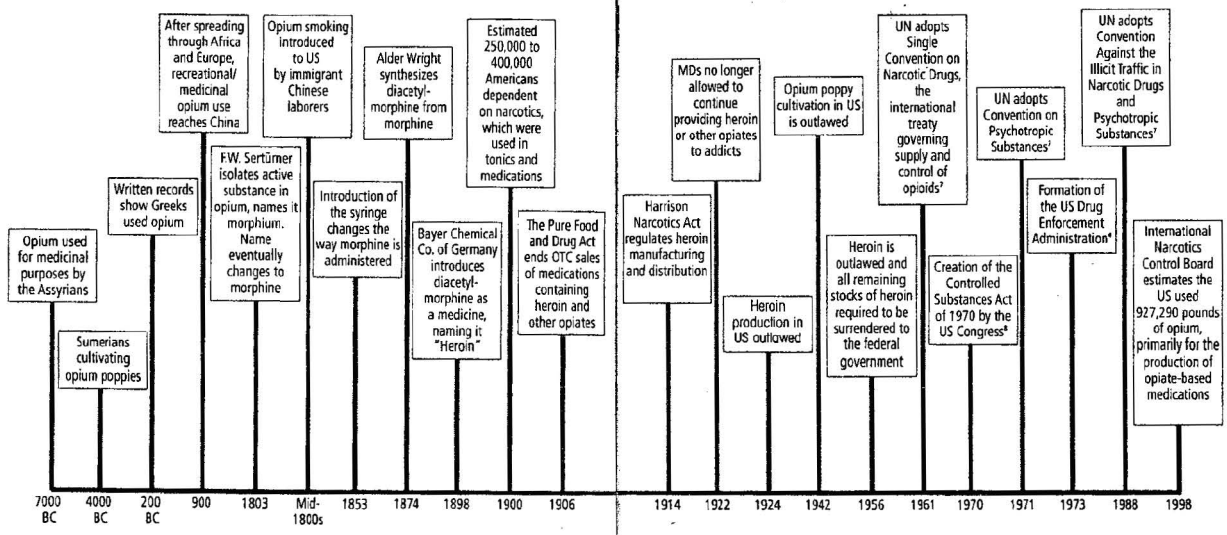
THE HISTORY OF OPIOIDS

Opium and its derivatives have been around for thousands of years. Use of opioids dates as far back as 7000 BC.[6] It is important to note that almost all opioids available today, both legally and illicitly, share a common lineage beginning with the opium poppy.

Timeline of opiate and opioid use[6]



OPIOID CLASSIFICATION[9]

Opioids can be classified into three groups depending on how they are derived. The naturally occuring opioids are alkaloids derived directly from opium.[9] Most semisynthetic opioids are derived from relatively simple modifications of morphine or thebaine.[9] Synthetic opioids are produced using no naturally occurring opium alkaloids and are derived purely from chemical synthesis.

Naturally Occurring Opioids[9]	Semisynthetic Opioids[9]	Synthetic Opioids[9]
Morphine Codeine Thebaine	Hydrocodone Hydromorphone Oxycodone Oxymorphone Heroin Buprenorphine	Meperidine Methadone Fentanyl Pentazocine

The word **opioid** is a broad term that refers to all compounds related to opium.[9] The term **narcotic**, once used to refer to any drug that induced sleep, is today usually used in a legal context to refer to a variety of substances, not restricted to opioids, with abuse or addictive potential.[9]

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DEA SCHEDULES OF CONTROLLED SUBSTANCES

IMPORTANT INFORMATION FROM THE CONTROLLED SUBSTANCES ACT OF 1970[8]

More specific information available at:
www.deadiversion.usdoj.gov/21cfr/index.html

Type	Examples[8,10,11]	Prescription notes	Refill notes
Schedule I*	Marijuana, heroin, LSD	No prescribing permitted	N/A
Schedule II	Morphine, codeine, hydromorphone, oxycodone, oxycodone with acetaminophen, oxycodone with aspirin, oxymorphone, fentanyl, meperidine, methadone	Written only,† partial filling permitted in certain circumstances (may be transmitted via fax in certain circumstances)	No refills permitted
Schedule III	Codeine with acetaminophen, hydrocodone with acetaminophen, hydrocodone with ibuprofen, hydrocodone-containing elixirs, buprenorphine	Written, oral (promptly reduced to writing by pharmacist), partial filling permitted (may be transmitted via fax)	No prescription for a controlled substance listed in Schedule III or IV shall be filled or refilled more than six months after the date on which such prescription was issued and no such prescription authorized to be refilled may be refilled more than five times.
Schedule IV	Propoxyphene, propoxyphene with acetaminophen, phenobarbital, benzodiazepines	Written, oral (promptly reduced to writing by pharmacist), partial filling permitted (may be transmitted via fax)	
Schedule V	Diphenoxylate combination products, codeine-containing elixirs	Written, oral (promptly reduced to writing by pharmacist), partial filling permitted (may be transmitted via fax)	No restrictions listed

- The Controlled Substances Act, and its implementing regulations, can be accessed at **http://www.deadiversion.usdoj.gov/21cfr/index.html** on the Drug Enforcement Administration Web site.
- If there is a difference between federal and state law or regulation, the more restrictive applies. Please consult your state's controlled substance policy for more information
- For more information about prescribing requirements in your state, including prescription requirements for controlled substances, please contact your state medical board or state board of pharmacy

* Schedule I substances have no currently accepted medical use in the United States.
† Oral is allowed, but only in emergency situations, as defined by the Code of Federal Regulations. Some states have more restrictions than appear in federal regulations (e.g., emergency oral prescription of Schedule II opioids is not allowed under any circumstances in Kentucky).

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MEANINGFUL DEFINITIONS

IMPORTANT DEFINITIONS RELATED TO THE USE OF OPIOIDS FOR THE TREATMENT OF PAIN*[12,13]

Addiction: a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing development and manifestations; characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.[12]

Addiction is a disease. It is not caused by drugs; it is triggered in a susceptible individual by exposure to drugs, most commonly through abuse. The kind of drug, the person's environment, their psychological makeup, and other social factors can contribute to the risk of addiction.[13]

Physical dependence: a state of adaptation manifested by a specific drug class withdrawal syndrome produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or the administration of an antagonist.[12]

Physical dependence is a known effect of certain medications. Confusing physical dependence with addiction is a common error, caused by the fact that most people that health care or law enforcement professionals encounter with addiction are also physically dependent to the substance(s) they are abusing. Thus, withdrawal is frequently seen in these people, and it is easy to think that withdrawal equals addiction. The number of people who are physically dependent (i.e., at risk for withdrawal syndrome, if the medicines are abruptly stopped) on some type of medication (e.g., antihypertensives, decongestants) far exceeds the number of who are addicted to a drug that induces physical dependence. Discussion of the topic is also muddled because for many years addiction was called "psychological dependence" (not to be confused with physical dependence) and thus an addict was often said to be "dependent" on the drug.[13]

Tolerance: a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.[12] Tolerance may also develop with some opioid side effects, such as respiratory depression.[13]

Tolerance to the respiratory depressant effects of opioids is what allows a patient with pain to regularly take a dose of medicine that would be fatal for someone who wasn't taking the same medicine on a regular basis. Exceeding tolerance, by taking larger than usual doses or abusing a number of drugs simultaneously, can be fatal to the abuser.[13]

Pseudoaddiction: describes the misinterpretation by members of the health care team of relief-seeking behaviors in a person whose pain is inadequately treated as though they were drug-seeking behaviors as would be common in the setting of abuse. The lack of appropriate response to the behaviors can result in an escalation of them by the patient, in an attempt to get adequate analgesia. Patients with unrelieved pain may:[12]

- Become focused on obtaining medications
- "Clock watch"
- Display behaviors (eg, doctor shopping, deception) to obtain relief

Pseudoaddiction can be distinguished from addiction in that the behaviors resolve when pain is effectively treated.[12,14]

*** As recommended by the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine.**

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MEANINGFUL DEFINITIONS (CONT'D)

Addicts vs physically dependent patients: the differences[2]	
Addicts	**Physically Dependent Patients**
• Suffer from chronic, neurobiologic disease with genetic, psychosocial, and environmental components	• Experience normal response to ongoing use of certain medicines, including opioids or other substances
• Seek a drug in order to quickly affect the "reward center" of their brains	• Want sufficient medicine to reach opioid receptors in spinal cord, preventing pain signal from reaching brain
• Crave drugs and use them compulsively	• Take medicines to relieve symptoms—not to satisfy a craving
• Continue abuse despite negative, even life-threatening, physical, mental, and/or social consequences	• Can discontinue taking their medicine once their symptoms are gone by gradually tapering the dosage according to their doctor's orders

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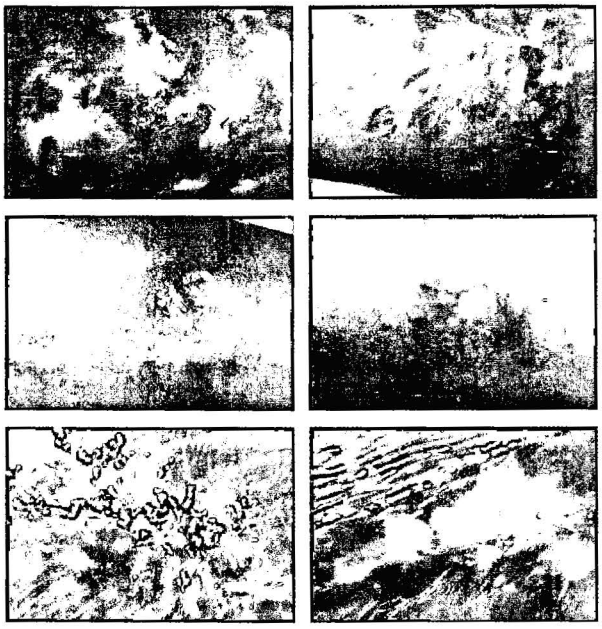
INDICATIONS OF POSSIBLE ABUSE

SIGNS THAT POINT TO POTENTIAL ABUSE PROBLEMS[15]*

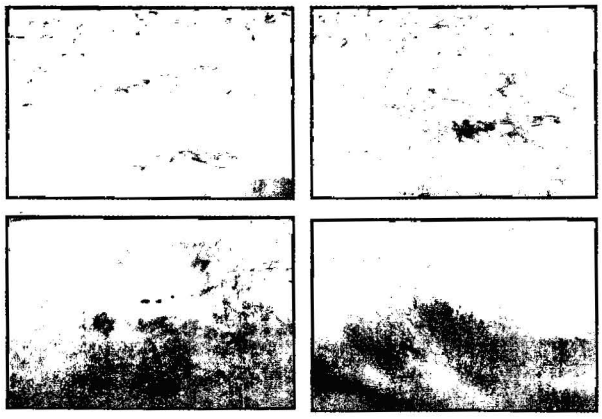
Some diverters are also abusers and are diverting to support their untreated abuse or addiction. Look for signs of drug abuse:

- Marks caused by injections

Skin popping (caused by injecting drugs under the skin)



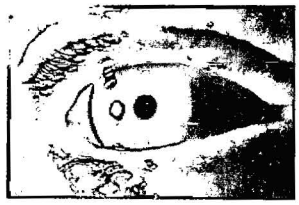
Track marks (arm) (rows of scars from repeated injections)



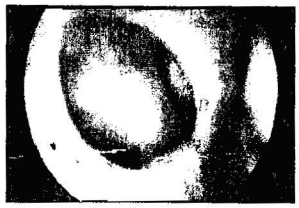
Track marks (neck)

Healing ulcer (leg)

- Constricted pupils



- Perforated nasal septum



(Healthy nasal septum)

Perforated Nasal Septum: In this patient, the photograph is taken through a speculum placed in the left nares. One of the left turbinates is visible in the far-right side of the photograph (where the light reflex is). The structure in the middle is in the septum, which allows the examiner to also view the right turinates through the septal perforation.

also:

- Loss of appetite
- Sniffles, watery eyes, cough, nausea
- Lethargy, drowsiness, nodding
- Possession of paraphernalia: syringes, bent spoons, needles

***While these signs usually suggest abuse, some of them may be associated with legitimate opioid use (e.g., pupillary constriction) or other medical therapy (e.g., track marks following an extended stay in a hospital). They should not be the only criteria for determining whether opioid abuse has occurred.**

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INDICATIONS OF POSSIBLE ABUSE (CONT'D)

BEHAVIORS OFTEN SEEN IN DRUG DIVERTERS

- Strange stories surrounding why they need medication[16]
- Reluctance to cooperate[15]
- Unusually high or low understanding of medications[16]
- Repeated episodes of lost or stolen prescriptions[17]
- Exaggerating or feigning symptoms[16]
- Specific drug requests[16]
- Use of multiple physicians or pharmacies[17]
- Wanting appointments toward the end of office hours[18]
- Calling or arriving after hours or when their primary physician is not available[18]
- Insistence on being seen immediately because they are late for another appointment[18]
- Not interested in having a physical examination, giving permission to obtain past records, or undergoing diagnostic tests
- Extremely slovenly or over-dressed
- Unwilling/unable to give name of regular physician; often claim to have no health insurance
- Reciting textbook symptoms or giving vague medical history

LAB SIGNS THAT MAY SUGGEST SUBSTANCE ABUSE[19]

- Elevated MCV
- Abnormal liver enzymes
- Unexpected results in urine drug testing (The use of this technology requires understanding of specificity and sensitivity of the particular analytic method employed. Some point-of-care urine tests for "opioids" or "opiates" do not, for example, detect semisynthetic or synthetic opioid analgesics. See page 22).

PROTECTING PRESCRIPTIONS

Whether you are a healthcare provider who prescribes controlled substances or a law enforcement officer in the position to advise prescribers, these steps may be useful in protecting prescriptions and curbing diversion:

- **Keep prescription pads locked away and secure.** This will reduce opportunities for theft.
- **Never sign an incomplete prescription.** Diverters are notorious for altering prescriptions or adding information that you do not intend
- **Write quantities and strengths in both numbers and letters.** This will prevent most attempts at altering the intended dose, quantity or strength.
- **Use tamper-resistant prescription pads.** For more information, contact your Purdue Pharma representative
- Write on the prescription the name of pharmacy where the patient wants to have it filled
- Consider faxing the prescription to the pharmacy for later comparison and authentication by the pharmacist
- Do not have medical license number or DEA registration number pre-printed on prescriptions. Write them each time they are required. This will make it harder for prescription pad thieves to successfully forge or counterfeit prescriptions.

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STRATEGIES FOR IDENTIFYING ABUSERS

ASK THE RIGHT QUESTIONS

These questions can be asked during the patient history

Method 1: The CAGE Questions[19]

One or more positive answers may indicate a problem with substance abuse.

1. Have you ever tried to **C**ut down on your alcohol or drug use?
2. Do you get **A**nnoyed when people comment about your drinking/drug use?
3. Do you feel **G**uilty about things you've done while drinking/using drugs?
4. Do you need a drink or a drug as an "**E**ye-opener"?

Method 2: The Trauma Test[20]

Two or more positive answers (or 2 or more accidents) may indicate a problem with substance abuse.

Since your 18th birthday, have you...

1. Had any fractures/dislocations of bones or joints (excluding sports injuries)?
2. Been injured in a traffic accident?
3. Injured your head (excluding sports injuries)?
4. Been in a fight or assaulted while intoxicated?
5. Been injured while intoxicated?

BE ON THE LOOKOUT

Warning indicators of a possible problem with drug abuse

- Atrophied or perforated nasal septum[19]
- Sexually or needle-transmitted diseases[20]
  - — Endocarditis
  - — Hepatitis
  - — HIV/AIDS
- Complaints of sexual dysfunction with no other cause found[20]

Note: Appearance of these indicators serve to alert you to potential problems. They do not mean you should withhold appropriate care.

WHAT TO DO

How to handle a patient whom you suspect of addiction or drug abuse[8]

- Remember, a person abusing drugs or addicted is in need of treatment
- Refer the patient to an addiction specialist or treatment center if warranted
- If you are not the primary care physician, always consult a patient's regular physician before initiating treatment with an opioid analgesic.
- Contact authorities if you are threatened in any way

Identifying patients with drug abuse problems will help you direct them to appropriate care. It also helps ensure that those with legitimate medical need for opioid medications will be able to obtain them.

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DRUG TESTING

Urine is currently the most widely used and extensively validated biologic specimen for drug testing.[18] This information should serve as an overview of things you should look for or ask for with urine drug testing (UDT)

TWO MAIN TYPES[18]:

1. Immunoassays (laboratory-based or at point-of-care [POC])
   - Generally detect classes of drugs
   - Classify substances as present or absent
   - False-positive and -negative results can occur
     - — Cross-reaction can occur with structurally similar or unrelated drugs
     - — Opiate immunoassays may not reliably detect synthetic or semisynthetic opioid analgesics (such as methadone or oxycodone). The appropriate use of these assays requires an understanding of the sensitivity and specificity of the test with regard to a specific drug.
2. Laboratory-based specific drug identification (e.g., gas chromatography/mass spectrometry [GC/MS], high-performance liquid chromatography [HPLC])
   - Identifies individual drugs and drug metabolites
     - — No cross-reaction
   - A therapeutic drug level may fall below a test's cutoff concentration
     - — Do not assume a negative result means no drug is present
     - — Ask for "no threshold" testing
   - There is no consistent relationship between dose and urine concentration of a drug or its metabolites.

BEFORE ORDERING A TEST[18]

- Ask the patient:
  - — Are you taking any prescription, OTC, or herbal medications or products?
    - When was the last dose/use?
  - — Drug abuse history
- Let the laboratory know:
  - — Medications that the patient is taking
  - — What you are looking for:
    - Illicit substance
    - Prescription drug use or misuse

PRACTICAL STRATEGIES[18]

- Select testing laboratory or POC device supplier
- Select routine UDT panel for commonly abused drugs:
  - — Recommended immunoassay screens[18] are:
    - Cocaine
    - Amphetamines (including ecstasy)
    - Opiates
    - Methadone
    - Marijuana
    - Benzodiazepines
  - — Additional tests, as needed
  - Drug identification:
  - — GC/MS or HPLC for all patients prescribed opioids
    - Specify "no threshold" to increase likelihood of detecting prescribed medications
- Specimen collection:
  - — Random collection preferred
  - — Unobserved specimen collection usually acceptable
  - — Temperature testing should be routine, regardless of method of assay. Creatinine concentration and specific gravity should be routinely determined when specimens are sent to a laboratory.

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DRUG TESTING (CONT'D)

- UDT results:
  - — Anticipate what you will do with results
  - — A positive UDT result reflects recent drug use
  - — Use a negative result for prescribed medication to initiate a dialogue with patient to preserve therapeutic alliance
    - Schedule appointment to discuss abnormal or unexpected results with patient
    - Use results to strengthen doctor-patient relationship and support positive behavior change
  - — Document results and interpretation
  - — Understand what you are looking for
    - UDT may detect other opioids that were not prescribed. These may have been taken by the patient or may be metabolites of the drug(s) prescribed (e.g., codeine is partially metabolized to morphine; hydrocodone may be partially metabolized to hydromorphone; morphine may be partially metabolized to hydromorphone; oxycodone is partially metabolized to oxymorphone).

ADDITIONAL TESTING METHODS[18]

Factors influencing the type of drug test to choose are ease of specimen collection, analytical/testing considerations, and interpretation of results. These tests are new, and there are limitations (eg, false-positive/false-negative results, interferences, and cross-reactivity).

Method	Pros	Cons
Saliva	Ease of sample collection Minimal personal invasiveness Limited preanalytical manipulation	Drugs and/or metabolites generally retained for shorter period and at lower concentrations than in urine
Hair	Retrospective, long-term measure of drug use directly related to hair length	Dark hair has greater capacity to bind drug than fair/gray hair (bias) Irregular growth Labor-intensive sample preparation
Sweat	Noninvasive, cumulative measure of drug use over days/weeks Most appropriate in monitoring drug use in chemical dependency or probation programs	Varying sweat production Risk of accidentally removing or contaminating collection device
Blood	More accurate determination of drug concentrations provided by quantitative analysis	Not amenable to rapid screening Not recommended for routine testing

- More complete information on urine drug testing can be downloaded from the California Academy of Family Physicians public Web site:

http://www.familydocs.org/files/UDTmonograph.pdf and http://www.familydocs.org/assets/Professional_Development/CME/UDT_Ref_Card.pdf

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RESOURCES

The following resources can provide important information on prescription pain medications, their identification, their appropriate use, and drug abuse and diversion.

- The American Pain Society (APS): www.ampainsoc.org
- American Academy of Pain Medicine (AAPM): www.painmed.org
- American Society of Addiction Medicine (ASAM): www.asam.org
- Pain and Policy Studies Group of the University of Wisconsin Comprehensive Cancer Center: www.painpolicy.wisc.edu
- Drug Enforcement Administration: www.deadiversion.usdoj.gov
- Food and Drug Administration: www.fda.gov
- The Substance Abuse and Mental Health Services Administration (SAMHSA): www.samhsa.gov
- The National Association of Drug Diversion Investigators (NADDI): www.NADDI.org
- Dads And Mad Moms Against Drug Diversion: www.DAMMADD.org
- Local law enforcement
- Local addiction treatment specialists/centers

REFERENCES

References: 1. Promoting pain relief and preventing abuse of pain medications: a critical balancing act. A joint statement from 21 health organizations and the Drug Enforcement Administration [Press release]. US Drug Enforcement Administration, Washington, DC, October 23, 2001. **2.** American Academy of Pain Medicine and American Pain Society. The use of opioids for the treatment of chronic pain: consensus statement from the American Academy of Pain Medicine and the American Pain Society. Glenview, Ill. 1997. **3.** Ellison NM, Lipman AG, Patt RB, Portenoy RK. Opioid analgesia: an essential tool in chronic pain. *Patient Care*. July 15, 1998;47-66. **4.** Drug Enforcement Administration. Physician's Manual: An Informational Outline of the Controlled Substance Act of 1970. Revised 1990. Available at: http:// www.vetmed.wsu.edu/pharmacy/VM522P/controlled/Dea_all.htm. Accessed June 4, 2007. **5.** The American Bar Association Commission on Legal Problems of the Elderly: report to the house of delegates—Proposed ABA Policy on Legal Obstacles to Effective Pain Management. F.W. McCalpin, Chair. April 2000. **6.** Marnell T. Drug Identification Bible 4th ed. Ameri-chem, Inc. March 1999. **7.** United Nations Office on Drugs and Crime. UN Treaties and Resolutions. The three UN drug control conventions. Available at: http://www.unodc.org/unodc/en/drug_and_crime_conventions.html. Accessed June 4, 2007. **8.** Controlled Substances Act, Section 812. US Drug Enforcement Administration Web site. Available at: http://www.deadiversion.usdoj.gov/21cfr/21usc/index.html. **9.** Gutstein HB, Akil H. Opioid analgesics. In: Hardman JG, Limbird LE, eds. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 10th ed. New York, NY: McGraw-Hill. 2001:569-619. **10.** Goldman B. Preventing drug diversion: a program for physicians, study guide. Home Study Educators; 2001. **11.** Medical Economics Co., Inc. Physicians' Desk Reference®, PDR® Electronic Library™ (see respective product names). Available at: http://www.pdr.net. Accessed June 4, 2007. **12.** American Pain Society. Definitions related to the use of opioids for the treatment of pain. Available at: http://www.ampainsoc.org/advocacy/opioids2.htm. Accessed June 4, 2007. **13.** Purdue Bulletin for Law Enforcement Officers, Vol. 1. Useful facts about pain medications. Purdue Pharma. Stamford, Conn. May 2002. **14.** Weissman DE, Haddox JD. Opioid pseudoaddiction—an iatrogenic syndrome. *Pain*. 1989;36:363-366. Available at: http://ncadi.Samhsa.gov/govpubs/rpo926/ **15.** The National Clearinghouse for Alcohol and Drug Information. Drug categories for substance abuse. Available at: http://www.health.org/govpubs/rpo926/. Accessed June 4, 2007. **16.** Cole BE. Recognizing and preventing medication diversion. *Fam Prac Manage*. October 2001:37-41. **17.** Passik SD, Portenoy RK, Ricketts PL. Substance abuse issues in cancer patients. *Oncology*. 1998;12:517-521. **18.** Gourlay DL, Caplan YH, Heit HA. Urine drug testing in clinical practice: dispelling the myths & designing strategies. San Francisco, Calif, The California Academy of Family Physicians and PharmaCom Group Inc. November 2006. **19.** Ewing, JA. Detecting Alcoholism: The CAGE Questionnaire. *JAMA* 252: 1905-1907, 1984. **20.** Weaver MF, Jarvis MAE, Schnoll SH. Role of the primary care physician in problems of substance abuse. *Arch Intern Med*. 1999;159:913-924. **21.** Thummel KE, Shen DD. Design and optimization of dosage regimens: pharmacokinetic data. In: Hardman JG, Limbird LE, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 10th ed. New York, NY: McGraw-Hill, Inc; 2001:1917-2023.

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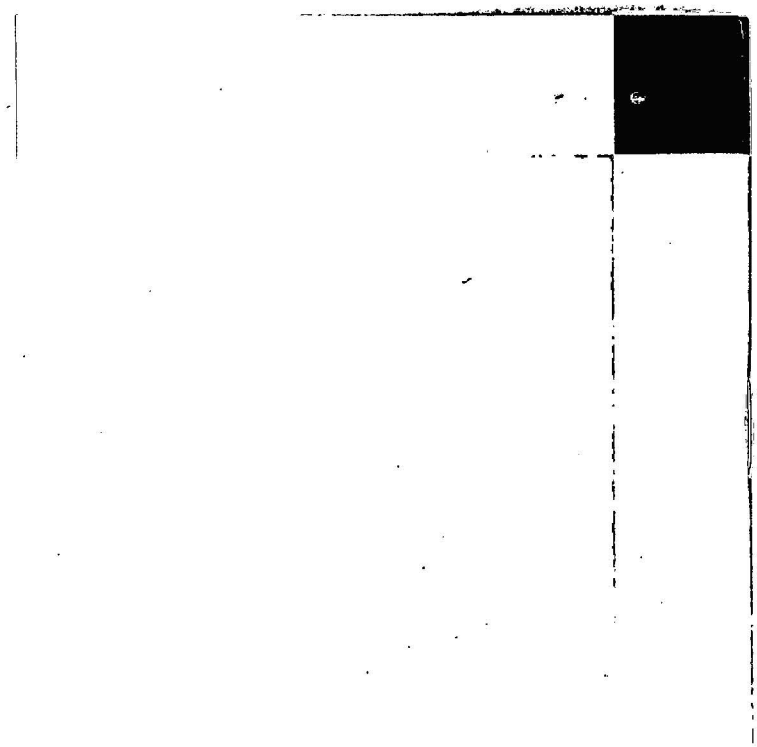

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This brochure is a general guide intended as a reference for medical and law enforcement professionals. It should not be used as a sole resource or in lieu of clinical or professional judgment.

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